Response Under 37 CFR §1.116
Expedited Procedure
Group 1804

ATTORNEY DOCKET NO. 1414.087
PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of	)	
	)	
FINKEL et al.	)	
	)	Group Art Unit: 1804
Serial No. 08/136,113	)	
	)	Examiner: Railey, J.
Filed: October 13, 1993	)	
	)	
For: "EFFICIENT AND SELECTIVE ADENOVIRAL-MEDIATED GENE TRANSFER INTO VASCULAR NEOINTIMA"	)	

DECLARATION

BOX AF
Assistant Commissioner for Patents
Washington, D.C. 20231

NEEDLE & ROSENBERG, P.C.
Suite 1200, The Candler Building
127 Peachtree Street, N.E.
Atlanta, Georgia 30303-1811

November 3, 1995

I, Toren Finkel, M.D., Ph.D., declare as follows:

1. I am the Toren Finkel named as an inventor in the above-identified application.

2. I have worked in the field of adenoviral-mediated gene transfer for 3 years and have authored about 4 papers in this area of study.

3. The proteins and antisense RNA molecules included in claims to methods for treating restenosis in the above-identified application, *i.e.*, herpes simplex virus thymidine kinase, dominant negative ras gene product, nitric oxide synthase (proteins), and c-myc, c-myb, CDC2 and PCNA (antisense RNAs), are known in the art to be cytotoxic or inhibitory to cell proliferation when transfected into cells.

4. Because the above-named proteins and antisense RNAs are known to be cytotoxic or inhibitory to cell proliferation, it is more likely than not that when the genes encoding these molecules are transfected into neointimal cells, they will be cytotoxic or cause a decrease in proliferation of neointimal cells.

5. Restenosis is known to be caused by injury to blood vessels wherein medial smooth muscle cells are activated, begin to migrate, and proliferate to form a neointima.

6. Because restenosis is caused by the proliferation of neointimal cells, causing a decrease or inhibition of neointimal cells is reasonably expected to treat, *i.e.*, prevent or decrease the severity of, restenosis.

7. Therefore, it is credible that when the genes encoding herpes simplex virus thymidine kinase, dominant negative ras gene product, nitric oxide synthase (proteins), and c-myc, c-myb, CDC2 and PCNA (antisense RNAs) are transfected into neointimal cells, they will treat, *i.e.*, prevent or decrease the severity of, restenosis.

8. The conclusion in (7) above is further based upon the example provided in the application wherein the treatment including selective expression of thymidine kinase in neointimal cells in combination

with treatment with ganciclovir was shown to be effective in treating restenosis in the rat corotid artery injury model.

9. Based upon this same reasoning and example, it is also credible that other nucleic acids whose gene products are cytotoxic or cause a decrease in proliferation of neointimal cells will work in the present method to treat restenosis.

10. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine, imprisonment, or both, under U.S.C. Title 18, § 1001, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

11/6/95

Toren Finkel date

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